Remarks

Claims 1 through 9 are pending in this application. In the Response to Restriction Requirement filed October 9, 2007, Group I, containing Claims 1 through 9 and 11, were elected with traverse. Claims 10 and 11 were previously cancelled by Preliminary Amendment, concurrent with the Response to Restriction Requirement. The pending claims stand rejected under 35 U.S.C. §112, second paragraph and 35 U.S.C. §103. This paper contains amendments under 37 C.F.R. §1.121.

Rejection of Claims 1 through 3, 5, and 7 under 35 U.S.C. §112, Second Paragraph

Claims 1 through 3, 5, and 7 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. As suggested by the Office, Claims 1 through 3, 5, and 7 are currently amended to alter the term "and the pharmaceutically acceptable salts thereof" to instead read in the alternative using the term "or a pharmaceutically acceptable salt thereof." As such, Applicants assert that Claims 1 through 3, 5, and 7 are not indefinite. Applicants further assert that the rejection is obviated and respectfully request withdrawal of this rejection.

Rejection of Claims 1, 7, and 8 under 35 U.S.C. §103(a)

Claims 1, 7, and 8 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Reuveni et al. (Reference CA) in view of Peptor, LTD. (Reference BA; WO 01/91754, the '754 patent application). Applicants respectfully disagree with this rejection.

The factual inquiries set forth in *Graham v. John Deere Co.,* 383 U.S. 1 (1966) are employed when making an obviousness analysis. Those factual inquiries include: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the prior art and the claims in issue; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary considerations. A finding of obviousness under 35 U.S.C. §103(a) requires that the prior art suggest the claimed invention, as a whole, to one of ordinary skill in the art. Thus, the obviousness inquiry of 35 U.S.C. §103(a) requires a factual comparison of the claimed subject matter to the relevant art. To render a claim obvious, the prior art must be such as to lead one of ordinary skill in the art to arrive at the claimed invention with a reasonable expectation of success. (See MPEP 2141 I. and II.)

The Office points to a compound disclosed in Reuveni et al. on page 1030[8], Table 1, first column (fourth compound from the top of the table) and notes that "[t]he difference between

the prior art compounds and the instantly claimed compounds is the 7-position of the isoquinoline ring which represents phenyl." The Office then indicates that Peptor, LTD. teaches a similar class of isoquinoline compounds (see claims of the '754 patent [application]) and states that [a]t the 7-position of the isoquinoline ring, Peptor, LTD. teaches the equivalency of hydrogen and phenyl" (see radical R_5). The Office then asserts that it would have been obvious to the skilled artisan to replace the 7-hydrogen in a compound of Reference CA with a known equivalent such as 7-phenyl in view of the teaching of equivalence and the expectation of similar pharmaceutical properties. As noted above, Applicants respectfully disagree with this rejection.

While Reuveni et al. provides the compound noted by the Office on page 1030[8], "[s]ubstitutions on the A core (i.e. the 5-isoquinoline moiety) also diminished inhibition, possibly implying that the binding pocket is very tight at this region" (pp. 10309 through 10310, emphasis added). Thus Reuveni et al. specifically teaches away from adding any substitution, nevertheless phenyl at the 7 position, on the isoquinoline. Furthermore, Reuveni et al. points to NL-71-101 (see structure on page 10311), which has no substitution on the isoquinoline and an alkenylene linker between the amines in bridge B and the two phenyl moieties appended to the carbon, as showing the "best combination of selectivity and activity against PKB" of "all of the compounds examined" and being "a promising lead compound for further development of high affinity, selective PKB inhibitors" (see pp. 10314 and 10311). Applicants respectfully note that the present claims require a phenyl at the 7 position of the isoquinoline and lack an alkenylene linker between the bridging amines and the single phenyl moiety appended to the carbon. Thus, Reuveni et al. does not direct the skilled artisan toward the each of individual distinguishing elements noted for the present claims, nevertheless to these elements in their entirety. In fact, Reuveni et al. teaches away from the substituted isoquinoline and absence of an alkenylene linker in the present claims and, therefore, does not render the present claims obvious.

Turning to the '754 patent application, the '754 claims require the alkenylene linker between the Region B amines and the aromatic substituent group. While these '754 claims permit phenyl to be substituted at the 7 position on the isoquinoline, the preferred embodiments – which also include the alkenylene linker between the Region B amines and the aromatic substituent group – do not include any substitution on the isoquinoline when the single phenyl is presented for the aromatic substituent group and also require a non-hydrogen substitution on the carbon attached to that single phenyl (see Formula III, pp. 5 and 14). This same non-hydrogen substitution on the carbon attached to the phenyl is present in the '754 claims. The present claims for the pending patent application require phenyl at the 7 position on the isoquinoline, lack an

alkenylene linker, and permit only hydrogen substitution on the carbon attached to the phenyl. Additionally, improvements on the lead compound in the '754 application (B-11-1, which is the same compound as the lead in Reuveni et al. (NL-71-101)) do not have any substitutions on the isoquinoline, nevertheless phenyl at the 7 position, all retain the alkenylene linker, and possess a non-hydrogen substitution on the carbon when attached to a phenyl (see pp. 25 through 27). These points all demonstrate that the '754 patent application does not direct the skilled artisan to the present claims.

As for Reuveni et al. in view of the '754 patent application, Reuveni et al. teaches away from the substituted isoquinoline needed for the present claims and teaches toward an alkenylene linker which is not permitted by the present claims. When the skilled artisan takes Reuveni et al. and looks to the '754 patent application, the improvements on the lead compound as well as the preferred embodiments containing a single phenyl in the aromatic substituent group all lack any substitution on the isoquinoline. Furthermore, the improvements, noted preferred embodiments, and the '754 claims all require an alkenylene linker and a non-hydrogen substitution on the carbon attached to the phenyl. These teachings do not and cannot lead the skilled artisan to the present claims that require phenyl at the 7 position on the isoquinoline, do not possess an alkenylene linker, and permit only hydrogen substitution on the carbon attached to the phenyl.

In view of the aforementioned aspects of the cited references, Applicants respectfully assert that significant differences exist between the present claims and teaching supplied by these cited references. As clearly evidenced by these references, there is no teaching or suggestion whatsoever that would yield the present claims. Also, the cited references provide no motivation to make the multitude of changes necessary to arrive at the claimed compounds. Thus, Applicants respectfully request withdrawal of this rejection.

Information Disclosure Statement

Applicants acknowledge that the Office has considered the Information Disclosure Statement filed May 12, 2006.

Conclusion

Applicants assert that the above-stated remarks overcome the Office's rejection for this application. Applicants courteously solicit reconsideration of this rejection and passage of this case to issuance.

Respectfully submitted,

/Danica Hostettler/

Danica Hostettler
Attorney for Applicants
Registration No. 51,820
Phone: 317.276.3711

Eli Lilly and Company
Patent Division
P.O. Box 6288
Indianapolis, Indiana 46206-6288

March 26, 2008